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**Outcome study of the Pipeline Embolization Device
for treatment of intracranial aneurysms at a single UK institution**

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Outcome study of the Pipeline Embolization Device for treatment of intracranial aneurysms at a single UK institution

Abstract

Background: The introduction of flow-diverting stents in the last decade provides an alternative endovascular treatment choice in selected intracranial aneurysms. This retrospective analysis of a UK centre's experience provides insight into clinical and radiographic outcomes.

Methods: Electronic patient records, diagnostic and procedural images and written procedural records for patients treated with the PED between August 2009 and April 2014 were reviewed. Follow-up TOF MRA was performed after treatment. Clinical and radiographic outcomes were analyzed and compared with other PED studies.

Results: Twenty-nine patients with 30 attempted PED treatments were reviewed representing 3.5% of the treated aneurysm patient cohort. 63.6% (21/33) of the aneurysms were wide-necked (> 4 mm), 60.6% (20/33) were large or giant (≥ 10 mm). The mean aneurysm sac diameter was 12.0 mm; the mean neck width was 4.5 mm. Mortality and morbidity rates were 3.3% and 10.0%, respectively. The total adequate occlusion rate was 78.1% (25/32) at 18 months. The neck width of aneurysms with residual sac filling and complete occlusion differed significantly ($P = 0.04$).

Conclusion: Highly selected aneurysms treated with a PED in a UK centre have similar occlusion and complication rates when compared to non-UK studies. Again, it appeared that delayed aneurysm rupture remained a risk for PED treatment in large or giant aneurysms. Follow-up with TOF MRA gave similar occlusion results compared to those obtained with DSA in other studies. The influence of neck size on occlusion rate should be examined in future PED studies.

Keywords: PED, FDDs, endovascular treatment, intracranial aneurysm

Introduction

Endovascular coil embolization is the treatment of choice for many intracranial aneurysms although limitations include technical difficulty for complex cases and recanalization of large and giant aneurysms.^{1,2} The introduction of Flow-Diverter Devices (FDDs) in the last decade has provided an alternative endovascular treatment choice consisting of reconstruction of the diseased parent artery and induction of aneurysmal thrombus.^{3,4} FDDs have been widely used to treat large, complex, and uncoilable aneurysms with promising outcomes.⁵⁻¹² Currently, only device type⁶ and aneurysmal size and location⁸ have been identified as playing a role in efficacy and safety of FDDs treatment respectively. Whilst many non-UK retrospective and prospective studies of FDDs, including the Pipeline Embolization Device (PED, Covidien, Irvine, California), have been published, no randomized trials have been fully completed.¹³ We describe here a pragmatic and independent UK study into clinical and radiographic outcomes of PED implantation. Whereas most previous studies only used DSA to follow-up FDD-treated aneurysms, MRA was performed here.

Methods

In this retrospective study we reviewed electronic patient records (iSOFT, Falls Church, US), diagnostic and procedural images on the patient archiving and communication system (General Electric Healthcare, Waukesha, USA) and written procedural records for PED-treated patients at King's College Hospital, UK between August 2009 and April 2014. Data on aneurysm size and location were obtained from DSA (Allura Xper FD, Philips Healthcare, Amsterdam, Netherlands) and CTA (Lightspeed 16; General Electric Healthcare) by a core laboratory independent of those who performed the procedures (Y.S-H.).

Treatment

All cases were treated electively following a consensus decision at a neurovascular multi-disciplinary team meeting which included interventional neuroradiologists and neurosurgeons. A high probability of recurrence, a high neck diameter: sac diameter ratio, and increased neurosurgical technical difficulty were the factors leading to PED treatment in preference to coiling, stent-assisted coiling or neurosurgery. Patients were pre-medicated with aspirin and clopidogrel (75 mg PO OD for 7 days). Post-procedure medications were aspirin lifelong and clopidogrel for 6 months (75 mg PO OD). Platelet function testing is not performed at our institution as there is no proven clinical benefit.^{14–16}

PED placement procedures were performed under general anaesthesia using biplane angiography. A 6 F guiding-catheter system (Flexor Shuttle Select, Cook Medical, Bloomington, US) was placed into the distal cervical segment of the ICA ipsilateral to the target aneurysm or a distal V2 segment (Guider Softip, Boston Scientific, Natick, US; Neuropath, Codman, Raynham, US). A 0.027 inch microcatheter (Rebar 27 in first case, otherwise Marksman; both Covidien) was advanced past the neck of the target aneurysm using different microguidewires as necessary (Synchro 14, or Transend EX Platinum; Boston Scientific). The PED was delivered through this microcatheter and deployed across the aneurysm neck. A tri-axial system, incorporating a 0.058 inch intracranial support catheter (ReFlex A+, Reverse Medical, Irvine, California; Navien A+, Covidien), was used in both the anterior and posterior circulation from June 2012.

Follow-up

Post-treatment follow-up 3D TOF MRA (SIGNA 1.5 T HDX, General Electric Healthcare) with TR 23 ms, TE 2.5 ms, flip angle 20 (with ramped pulse), matrix 320 x 224, field of view 19 x 19 cm, slice thickness 1.4 mm (reconstructed to 0.7 mm), was performed within 12 months after treatment. If there were new clinical features developing during follow up, an earlier MR (including MRA) or CT (including CTA) was performed depending on the clinical features. Further follow-up after 12 months was scheduled by the neurovascular multi-disciplinary team according to the follow-up image and the clinical outcome.

All adverse events were reviewed on an intention-to-treat basis. In order to compare our results with the largest clinical study of PED to date (International Retrospective Study of the Pipeline Embolization Device¹⁷), we used the same adverse event classification. An ongoing clinical event at 7 days following the event was defined as a “major” adverse event. Other events that resolved within 7 days with no clinical sequelae were defined as “minor” adverse events.¹⁷

Results

Patient and aneurysm characteristics

Twenty-nine patients with 30 attempted PED or double-PED treatments were identified (Table 1). The mean age was 52 years (range 26–76) and 79.3% (23/29) of patients were women. There had been prior treatment of the target intracranial aneurysm with coils in 34.5% (10/29) of patients.

Sixty-four percent (21/33) of the aneurysms were wide-necked (> 4 mm), 57.6%

(19/33) were large (≥ 10 mm), 3% (1/33) were giant (≥ 25 mm) and 6.1% (2/33) were dysplastic fusiform aneurysms. The mean aneurysm sac maximal diameter was 12.0 mm, and mean neck width was 4.5 mm. Among the 13 aneurysms < 10 mm in this study, 2 were fusiform, 7 were saccular with a dome: neck ratio < 1.5 and the remaining had recurred following treatment and were technically difficult to treat by other means. In such scenarios our multi-disciplinary team considered it acceptable to treat aneurysms < 10 mm as this has been demonstrated in seminal FDD treatment studies^{4,17} as well as the first level 1 evidence study for PED safety and efficacy (the FIAT randomized-control trial) where there were a similar number of cases < 10 mm compared to the current study (41%).¹³

[Table 1 near here]

Periprocedural clinical outcomes

A total of 30 attempted PED procedures were performed for the 29 patients with 33 target aneurysms. One patient who had received one treatment for a left ICA paraophthalmic segment aneurysm had another PED procedure for right-sided aneurysms located in the ICA cavernous and paraophthalmic segments 2 months later. Three patients each received 2 PEDs for 1 target aneurysm in a single procedure, thus a total of 33 individual device deployments were attempted in the 30 procedures.

Device-deployment success (release of PED at target site) was achieved in 32 of 33 (97.0%) attempted PED deployments. The PED could not be delivered to the target

zone in 1 patient due to adverse arterial morphology. Of 28 treated patients, 3 had 2 aneurysms treated with a single PED.

Periprocedural mortality was 1/30 (3.3%) of PED procedures (Table 2). One patient had an acute aneurysmal rupture 2 days after successful PED deployment of a right ICA terminal segment carotid aneurysm, which caused a right middle cerebral artery (MCA) territory infarct, mass effect and ultimately death 6 days after the procedure. There was no adjunctive coil deployed with this PED. This aneurysm was the largest (30 mm) in this study and the only giant aneurysm.

The number of periprocedural stroke/TIAs was 1/30 (3.3%). One patient with a treated mid-basilar aneurysm had bilateral small infarctions in the pontine tegmentum, which caused right-sided hemiparesis, dysarthria, and ataxia (mRS = 4), hours after the procedure. He was treated with a glycoprotein IIb/IIIa receptor inhibitor (abciximab 10 mg IV) and discharged for further rehabilitation 16 days later with only minor dysarthria (mRS = 1).

There were 3/30 (10.0%) other periprocedural adverse events, which could plausibly be attributed to thrombosis and inflammation of the aneurysm. One patient developed diplopia with an ipsilateral sixth cranial nerve palsy on the day of the procedure. She was discharged home after 2 days and the ophthalmological follow-up a month later showed improvement in diplopia (mRS = 2). One patient had pre-treatment clinical features of headache and diplopia caused by a sixth cranial nerve palsy, which were exacerbated for 3 days after successful PED placement. The headache resolved, the diplopia improved and she was discharged home 7 days after the procedure. At

discharge and at 3 months ophthalmological follow-up, her mRS score was 1. Another patient suffered from headache (Universal Pain Assessment Tool, 6/10), which subsided the next day (mRS = 0), immediately after the procedure. All 3 patients had aneurysms in the anterior circulation and the maximal aneurysmal diameters were 16, 15 and 9 mm respectively. None of the patients with periprocedural neurological symptoms received steroid treatment because there is insufficient evidence to support its routine use.

The periprocedural neurologic morbidity was 6.7% (2/30) due to the two major adverse events¹⁷: the pontine tegmentum infarction causing dysarthria (mRS = 1) and the sixth cranial nerve palsy causing diplopia (mRS = 2). No periprocedural remote haemorrhage was found in this series.

[Table 2 near here]

MRA outcomes

Follow-up MRA (Table 3) was performed in 27/28 patients who had undergone technically successful procedures (1 patient died 6 days after the procedure). The mean follow-up time until the first MRA was 4.9 months (range 1 - 12).

Within 6 months

Of the 32 treated aneurysms, 3.1% (1/32) aneurysms ruptured before MRA. Within 6 months (first follow-up MRA was after 6 months in 4 patients), 65.6% (21/32) aneurysms achieved adequate occlusion (Raymond scale 1 or 2) or remodelling (in the 2 dysplastic fusiform aneurysms). Two patients with occluded aneurysms at the

end of this study were assumed to be non-occluded at this time point due to the first follow-up MRA being performed at 8 and 12 months, respectively.

Residual aneurysm sac filling (Raymond scale 3) was noted in 18.8% (6/32) of aneurysms at 6 months (or 25% (8/32) if the 2 patients whose first follow-up imaging at 8 months showed residual sac filling, were assumed to show the same at 6 months). Two of these were recurrent aneurysms that had been treated with coils before PED treatment. Another 2 of these had undergone adjunctive treatment with coils in the same session of PED placement. Two were pseudoaneurysms (including one of the previously coiled aneurysms), which had formed following meningioma resections.

Between 6 and 18 months

Between 6 and 18 months, 4 additional aneurysms were adequately occluded (Raymond scale 1 and 2). These included the 2 aneurysms in 2 patients who underwent the first follow-up MRA at 8 and 12 months; 2 aneurysms showing residual sac filling (Raymond scale 3) at 6 months became adequately occluded at 8 and 18 months respectively. The total adequate occlusion rate in this study at 18 months was 78.1% (25/32). The maximum sac diameter of aneurysms with residual sac filling (Raymond scale 3) and aneurysms that showed complete occlusion (Raymond scale 1) was not significantly different ($P = 0.30$, $t = 1.05$, $df = 29$, two-tailed Student's t -test; 13.3 (5.0 - 24.0) mm (mean, range) vs. 10.8 (2.0 - 21.0) mm). The neck width of aneurysms with residual sac filling (Raymond scale 3) was significantly larger than those with complete occlusion (Raymond scale 1) [$P = 0.04$, $t = 2$, $df = 29$; 5.5 (3.0 – 6.5) mm vs. 4.0 (2.0 - 7.0) mm].

[Table 3 near here]

Among the remaining 6 aneurysms with residual sac filling at the end of this study (Table 4), the mean follow-up period was 28.5 months (range 8 – 62). One had a superior cerebellar artery arise from the aneurysm neck. We placed adjunctive coils in 34.4% (11/32) of PED deployments of which 82% (9/11) were adequately occluded [compared to 78% (25/32) overall].

[Table 4 near here]

Clinical outcomes at one year

Three patients had new neurological clinical features between discharge and one-year follow-up (none of whom had a periprocedural event) (Table 2).

The number of stroke/TIAs in the follow-up period was 2/30 (6.7%). Both resolved within 7 days with no clinical sequelae (classed as minor events). One of these patients discontinued clopidogrel 4 months after PED placement for a right ICA terminal segment aneurysm. He developed contralateral leg hemiparesis secondary to a small ipsilateral basal ganglia infarction (mRS = 4). The clinical features were self-limiting and he was discharged home 3 days later (mRS = 0). Another patient had one TIA presenting as left-sided hemiparesis (mRS = 4) 8 months after the PED procedure and 2 months after she had stepped down to anti-platelet mono-therapy. The MRI demonstrated a tiny infarct in the right peritrigonal region as well as complete occlusion of the PED-treated aneurysm (previously Raymond scale 3 at 6 months). This ischaemic event could be related to final thrombosis of the aneurysm. This

patient received a short course of dual-anti-platelets and was discharged home that day without further events.

Neurological clinical features not caused by a stroke/TIA were seen in a further patient 1/30 (3.3%) who had a 20 mm left ICA terminal segment aneurysm (Raymond scale 3). At 3 months after the procedure, the aneurysm increased in size to 28 mm and caused mass effect with clinical features of short-term memory impairment (mRS = 2). Clopidogrel was discontinued and the symptoms improved (mRS = 1). The follow-up MRA 1 month later showed a decrease in the overall size of the partially-thrombosed aneurysm with no change in the size of the residual sac. New onset seizures developed 3 years after PED treatment and the residual sac was coiled. However, following the retreatment, the patient continued to experience seizures.

The overall cumulative mortality and residual morbidity rates were 3.3% and 10.0%, respectively. There were 7 adverse events from a total of 29 (24.1%) aneurysms of the anterior circulation, including one death. There was one adverse event (ischaemic stroke) from a total of 3 (33.3%) posterior circulation aneurysms.

Discussion

The enrolled twenty-nine patients represented just 3.5% of the treated aneurysm patient cohort because cases were highly selected on the basis of a high probability of recurrence, a high neck diameter: sac diameter ratio, and increased neurosurgical technical difficulty. No other papers have reported, to the best of our knowledge, such a highly selected group (Supplementary Table 1).^{4,5,7,9,10,19–22}

Occlusion rates

Previous published complete occlusion (Raymond scale 1) rates of aneurysms treated with flow-diverter devices (FDDs) ranged from 55-95% over various follow-up intervals.^{23,24} When compared with PED-only studies, the complete occlusion rate of our study was 65.6% at 6 months, which was lower than the 91.2% at 6 months demonstrated previously.²⁴ Recently, a meta-analysis incorporating 1451 patients with 1654 aneurysms treated with FDDs demonstrated a complete occlusion rate of 76% (95% CI, 70%–81%) at 6 months.⁸ When compared with PED-only studies, the complete occlusion rate of our study was 78.1% at 18 months (mean duration to occlusion: 5.8 months, SD: 3.3 months) which was between the 86.8% at 1 year⁵ and the 57.4% at 10 months²⁵ reported previously.

A meta-analysis⁶ analyzing 897 patients with 1018 aneurysms treated with FDDs, showed that device type was the only variable causing a difference in the complete occlusion rate. The Silk device (Balt, Montmorency, France) had a significantly lower mean occlusion rate (defined as “complete or nearly complete occlusion of the treated aneurysm”) compared with the PED (68% and 88%, respectively; mean follow-up time: 9.0 months, SD: 6.6 months). In contrast, our study showed that the neck width of aneurysms with residual sac filling (Raymond scale 3) and complete occlusion (Raymond scale 1) at 18 months (mean: 5.8 months, SD: 3.3 months) differed significantly ($P = 0.04$). This is potentially related to the two treatment mechanisms of PED, one of which is inducing thrombosis in the aneurysm by reducing the exchange flow between the aneurysm and parent artery, and the other is providing scaffolding for neointimal overgrowth of the aneurysm neck^{26,27}. It is plausible that the wider the neck, the more the exchange flow which might reduce thrombosis and

hinder neointimal growth. At 180 days the only similar subgroup analysis⁵ demonstrated no difference in complete occlusion rate (Raymond scale 1 vs. Raymond scale 2 and 3) between those with a neck width ≥ 6 mm and those with a neck width < 6 mm. In our study, the occlusion rate between those with a neck width ≥ 6 mm and those with a neck width < 6 mm was significantly different [$P = 0.02$, 4/8 (50%) vs. 22/24 (91.7%) Fisher test].

Other than neck size, aneurysm sac diameter is generally considered a main factor influencing the occlusion and recurrence rate in endovascular treatment. In contrast to evidence from aneurysms treated with coiling, which suggests that smaller aneurysms have a higher occlusion rate (Raymond scale 1 and 2)²⁸, a meta-analysis of FDD treatment⁸ showed that occlusion rates are high regardless of aneurysm diameter [80% for small (< 10 mm), 74% for large (≥ 10 mm ≤ 25 mm), 76% for giant aneurysms (> 25 mm); $P = 0.8$].⁸ Our study also found that the sac diameter of occluded and non-occluded aneurysms did not differ ($P = 0.3$), and that the complete occlusion rate did not differ when small aneurysms (< 10 mm) were compared with large and giant aneurysms (≥ 10 mm) ($P = 0.2$). Another study showed that complete occlusion rates did not significantly differ⁵ between aneurysms > 25 mm and < 25 mm but we had insufficient data to make this comparison.

Another factor that may influence the occlusion rate in our study was the number of PEDs used per aneurysm. Additional PEDs were deployed to increase either the construct length or the mesh density. Most target aneurysms (30/33) at our institution required one PED per aneurysm (mean 1.09) and no more than two PEDs per aneurysm were used. In contrast, many studies used more PEDs per aneurysm, for example with means of 1.5 (range 1–4; 41.9% > 1 PED),⁴ 1.3 (range not available),²⁴

and 3 (range 1–15; 98.1% > 1 PED).⁵ Inter-institutional differences may be due to variation in judgment and technical difficulties.⁵ We found that in our study and others (Supplementary Table 1)^{4,5,7,9,10,19–22} correlation between institutional occlusion rate and mean number of FDDs per aneurysm was not significant (Spearman, $r = 0.4$; 2-tailed t test $P = 0.2$). Therefore, it is plausible that PED number is not a main variable affecting occlusion rate.

We placed adjunctive coils in 34.4% of PED deployments compared to, for example, 51.6%⁴, 32.4%²⁴, and 0.9%⁵ (an endpoint of the latter study was complete occlusion of the aneurysm without adjuncts) seen in other studies. We found that in our study and others (Supplementary Table 1) the correlation between institutional occlusion rate and adjunctive coil use was not significant ($r = 0.4$; $P = 0.2$) which was concordant with a study exploring this relationship.²² The anecdotal benefit of adjunctive coils for FDD treatment remains to be proved.

Among the 9 aneurysms in this study that had previously been coiled and then were retreated with PED, one had residual sac filling at the end of follow up. Currently there is no data showing that previous coiling would influence the occlusion rate following PED treatment. We found that the correlation between institutional occlusion rates and the number of previously coiled aneurysms in this and 8 other studies (Supplementary Table 1) was not significant ($r = 0.1$; $P = 0.77$). It appears that previous coiling does not influence PED treatment efficacy.

Although seminal studies, such as PITA⁴ and PUFS,⁵ used DSA to follow up PED-treated aneurysms, worldwide adoption of FDD brought about a widening range of

follow up methods and their time points.²⁹ There has not been a comprehensive evaluation of what is the optimal post-treatment method or methods²⁹ and MRA has been considered a suitable imaging modality for follow-up in FDD studies including the first level 1 evidence study for PED safety and efficacy (the FIAT randomized-control trial).¹³

We used 3D TOF MRA as a follow-up modality rather than DSA. 3D TOF MRA is highly accurate for detection of residual flow in coiled aneurysms³⁰ and according to one study it is more sensitive compared with DSA.³¹ In two studies,^{30,32} the sensitivity and specificity of TOF MRA for follow-up of coiled aneurysms were 84-86% and 92-98% respectively when using DSA as ground truth.

It is unclear whether data from MRA follow-up for coiled aneurysms can be extrapolated to PED-treated aneurysms as there may be differences. For example, in contrast to platinum coils, the PED can result in a marked local signal void due to a larger bimetallic surface area coverage and radiofrequency shielding^{33,34} which may cause false positive detection of in-stent stenosis.^{35,36} However, the impact of this potential overestimation of in-stent stenosis is negligible in our study as no in-stent stenosis was seen on the MRA follow-up.

Nonetheless, one concern using TOF MRA as a follow-up modality is the false positive detection of intra-aneurysmal residual flow, which has been recognised with TOF MRA due to T_1 -weighted hyperintensity of thrombus.³⁷ False positive detection of intra-aneurysmal residual flow in our study is likely to be very low as other sequences (T_2 -weighted) and scan planes (multi-planar reformat) were routinely reviewed and in our institution we have yet to discover a false positive after a

subsequent DSA. Furthermore, the use of cross-sectional imaging confirmed complete occlusion because decrease in size of aneurysm sac on cross-sectional imaging appears to be the single most consistent sign of durable aneurysm occlusion (likely implying full endothelialization of device construct and secondary exclusion of aneurysm from parent circulation), rather than intra-aneurysmal thrombosis without occlusion, which would appear on DSA as an apparently cured aneurysm.^{29,38}

Currently, there is insufficient evidence to suggest we change the follow-up MRA at our institution from TOF to contrast-enhanced MRA to obviate the drawbacks of TOF, although it is reported as more accurate in other studies (albeit there is no prospective data examining PED with MRA at 1.5 T).^{37,39} There is also insufficient evidence that DSA alone, with procedural complication risks, is the optimal modality for follow-up.²⁹ Nonetheless, a limitation of this study is that DSA was not performed for follow-up which would have allowed direct comparison of efficacy outcomes with many previous studies and provide complementary information.

Among the six aneurysms with residual sac filling in our study, one had a superior cerebellar artery arise from the aneurysm neck thereby maintaining aneurysm patency through flow demand.²⁴ Depending on rupture risk, it can sometimes be argued that this is acceptable and even a potential advantage of PED treatment (some flow disruption with maintenance of flow into the branch originating from the sac and partial occlusion of the aneurysm).

Two aneurysms with residual sac filling were post-operative pseudoaneurysms. Currently there is no high-level evidence comparing endovascular occlusion rates of

“true” aneurysms with pseudoaneurysms. One study of uncoilable pseudoaneurysms treated with Neuroform stents (Stryker, Kalamazoo, US), which exhibit some flow-diverting properties, demonstrated that 50% were completely occluded, 40% were partially resolved (unquantified authors definition) and 10% showed no change.⁴⁰ Due to the limited numbers of such cases in our study and others, it remains unclear whether a pseudoaneurysm is a predictive factor for residual sac filling after PED treatment.

One aneurysm with residual sac filling was located in the M1 segment of the MCA. In the U.S., the Food and Drug Administration approved PED for use only “in the internal carotid artery from the petrous to the superior hypophyseal segments”.⁴¹ In the UK, the National Institute for Health and Care Excellence (NICE) did not stipulate the anatomic location for PED placement.⁴² Currently there is no study directly comparing the safety and efficacy of PEDs placed in the MCA and ICA. The only study for PED treatment of MCA aneurysms demonstrated morbidity of 20% (demonstrated as mRS = 2) with 73% of aneurysms completely occluded at 12 months,⁴³ results which are not dissimilar to the current study. It is plausible that the use of PED in the M1 segment of two patients is unlikely to influence the outcome of this study.

Clinical outcomes

The overall mortality of this study was 3.3%, similar to the 3.8% seen in the IntrePED¹⁷ study. The one mortality in our study was caused by delayed rupture of a giant (30 mm) aneurysm two days after the procedure. In the IntrePED study, all the aneurysms associated with delayed rupture were giant (undefined by authors) or large (≥ 10 mm), and giant aneurysms had the highest rupture rate of 4.5% compared with

0.5% and 0% for large and small (< 10 mm) aneurysms respectively.¹⁷ Intra-aneurysmal thrombosis is a possible cause of delayed aneurysm rupture after FDD treatment.⁴⁴ It was noted that both the one ruptured aneurysm in our study and all ruptured aneurysms in the IntrePED study were not treated with an adjunctive coil embolisation. Anecdotally, many interventional neuroradiologists use adjunctive coils with FDDs in giant aneurysms to reduce the risk of spontaneous aneurysm rupture,⁴⁵ however the mechanism for rupture hasn't been elucidated, nor is there evidence that adjunctive coils with FDDs avoid aneurysm rupture after treatment.^{6,8}

The overall morbidity rate (3 major adverse events in 30 procedures) was 10.0% in our study compared to 7.4% in the IntrePED study. One of the 3 major adverse events caused by enlargement of the partially-thrombosed aneurysm 3 months after treatment perhaps again highlights the higher complication risk associated with PED treatment of large or giant aneurysms.

Neither intraparenchymal haemorrhages nor parent vessel occlusions were observed in our study. The periprocedural stroke/TIA rate was 3.3%, which is lower than 6.5% in a study of equivalent size (2/31),⁴ and similar to the one month follow-up rate of 3.6% and 5% in two large meta-analyses of FDD treatment.^{6,8} The total cumulative stroke/TIA rate at 1 year follow-up in our study was 10.0% which was higher than the overall stroke rate of 6% and 4.7% demonstrated in the IntrePED study (median follow-up 19.3 months) and a recent meta-analysis⁸ respectively. However, the overall stroke rate of IntrePED didn't include minor events (symptoms resolving within 7 days without clinical sequelae). If minor events were excluded, the overall ischaemic stroke rate in our study would be 3.3%. We have changed our practice in an

attempt to reduce these potentially avoidable TIAs. First, patients wear a medic alert bracelet detailing that they are on anti-platelet medication and that a discussion with a neuroradiologist is required before any interruption of treatment. Second, they continue dual anti-platelets for 9 months, as opposed to 6 months, in light of recent indirect evidence.⁴⁶

A limitation of the study is the small number of cases. However, small numbers can be expected in a single centre study (NICE estimates that 60 PEDs are used in the entire UK per year)⁴² and even the seminal PITA study consisted of only 31 aneurysms.⁴ A strength of the study is that, to the authors' knowledge, it is the only UK publication analyzing PED safety and efficacy.⁴⁷ The lack of UK data was a particular challenge to the 2013 Medical Technologies Evaluation Programme performed by the UK's NICE. The results of this pragmatic study are likely to be generalizable to other UK centres with a similar operator number (2 performing PEDs), operator experience (7 and 6 years' experience at point of first deployment), neurovascular multidisciplinary team composition (2 neurosurgeons, 4 interventional neuroradiologists, 1 stroke neurologist) and population at risk (3.5 million in a unit treating 160-200 aneurysms per annum). Furthermore, the use of PEDs in the current study may be pertinent to UK local governance arrangements for new devices as well as the acceptability of local hospital business models.

Conclusion

Our pragmatic study demonstrated that intracranial aneurysms treated with a PED have similar occlusion and complication rates when compared with both systemic FDD meta-analyses and the largest PED study performed so far. This was despite our cases being highly selected on the basis of a high probability of recurrence, a high

neck diameter: sac diameter ratio, and increased neurosurgical technical difficulty, plausibly making the cohort morphologically challenging with a higher risk of residual filling and poor clinical outcomes. Again, it appeared that delayed aneurysm rupture remains a risk of PED treatment in large or giant aneurysms.

Follow-up with 3D TOF MRA appeared to give similar PED occlusion results when compared to those obtained with DSA in other studies. As shown in previous studies, aneurysm sac diameter did not influence the occlusion rate of PED treatment nor did the number of PEDs used for each aneurysm and the number of cases requiring adjunctive coils correlate with occlusion rate. We did find that aneurysmal neck size differed significantly between occluded and non-occluded PED-treated aneurysms, the clinical significance of which is unclear. This finding needs to be validated in larger studies.

Ethical statement

We received written confirmation from the Research and Development department at King's College Hospital NHS Trust, UK that the UK's Health Research Authority National Research Ethics Service does not require review by a Research Ethics Committee given the nature of the retrospective study using de-identified data nor was individual consent required. The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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Conflict of interest

There was no grant support for this study and the writing of the paper.

The authors declare that they have no conflict of interest.

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